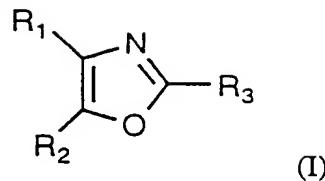


What is claimed is:

1. A compound of the formula:



5

wherein:

R₁ and R₂ are independently selected from an optionally substituted aryl or heteroaryl group, provided that at least one of R₁ and R₂ is an optionally substituted heteroaryl, and further provided that both R₁ and R₂ are not the same heteroaryl group;

10 wherein when one of R₁ and R₂ is an optionally substituted aryl ring, the ring is substituted by one or two substituents, each of which is independently selected, and which, for a 4-phenyl, 4-naphth-1-yl or 5-naphth-2-yl substituent, is halo, cyano, -C(Z)NR₇R₁₇, -C(Z)OR₂₃, -(CR₁₀R₂₀)_m COR₃₆, -SR₅, -SOR₅, -OR₃₆, halo-substituted-C₁₋₄ alkyl, C₁₋₄ alkyl, -ZC(Z)R₃₆, -NR₁₀C(Z)R₂₃, or -(CR₁₀R₂₀)_mNR₁₀R₂₀;

15 and which, for other positions of substitution, is halo, -(CR₁₀R₂₀)_m-cyano, -C(Z)NR₁₆R₂₆, -C(Z)OR₈, -(CR₁₀R₂₀)_m COR₈, -(CR₁₀R₂₀)_m"S(O)_mR₈, -(CR₁₀R₂₀)_m"OR₈, halo-substituted-C₁₋₄ alkyl, -C₁₋₄ alkyl, -(CR₁₀R₂₀)_m"NR₁₀C(Z)R₈, -(CR₁₀R₂₀)_m"NR₁₀S(O)_m'R₁₁, -(CR₁₀R₂₀)_m"NR₁₀S(O)_m'NR₇R₁₇, -(CR₁₀R₂₀)_m"ZC(Z)R₈ or -(CR₁₀R₂₀)_m"NR₁₆R₂₆;

20 and when one of R₁ and R₂ is an optionally substituted heteroaryl group, the substituent groups include one or two substituents each of which is independently selected from C₁₋₄ alkyl, halo, C₁₋₄ alkoxy, C₁₋₄ alkylthio, NR₁₀R₂₀, or an N-heterocyclyl ring which ring has from 5 to 7 members and optionally contains an additional heteroatom selected from oxygen, sulfur or NR₂₂;

25 R₃ is -X_aP(Z)(X_bR₁₃)₂, X_c or -(CR₁₀R₂₀)_n R₄;

R₄ is Q-(Y₁)_t;

Q is an aryl or heteroaryl group;

30 X_c is hydrogen, -(CR₁₀R₂₀)_n(Y₂)_p, -(CR₁₀R₂₀)_n-C=C-(CR₁₀R₂₀)_n(Y₂)_p, -(CR₁₀R₂₀)_n-C≡C-(CR₁₀R₂₀)_n'(Y₂)_p, or halosubstituted C₁₋₁₀ alkyl;

t is an integer having a value of 1 to 3;

p is 0 or an integer having a value of 1, provided that when p is 0 then Y₂ is hydrogen;

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X_a is -NR₈-, -O-, -S- or a C₁-10 alkylene chain optionally substituted by C₁-4 alkyl and optionally interrupted by -NR₈-, -O- or -S-;

X_b is independently selected from -(CR₁₀R₂₀)_n, -NR₈-, -O- or -S-;

Z is oxygen or sulfur;

5 n is 0 or an integer having a value of 1 to 10;
n' is an integer having a value of 1 to 10;
m is 0, or the integer 1 or 2;
m' is 1 or 2;
m" is 0 or an integer having a value of 1 to 5;

10 Y₁ is independently selected from hydrogen, C₁-5 alkyl, halo-substituted C₁-5 alkyl, halogen, -X_a-P(Z)-(X_bR₁₃)₂ or -(CR₁₀R₂₀)_nY₂;

Y₂ is halogen, -OR₈, -NO₂, -S(O)_m'R₁₁, -SR₈, -S(O)_m'NR₈R₉, -NR₈R₉, -O(CR₁₀R₂₀)_n'NR₈R₉, -C(O)R₈, -CO₂R₈, -CO₂(CR₁₀R₂₀)_n'CONR₈R₉, -ZC(O)R₈, -CN, -C(Z)NR₈R₉, -NR₁₀C(Z)R₈, -C(Z)NR₈OR₉, -NR₁₀C(Z)NR₈R₉,

15 -NR₁₀S(O)_m'R₁₁, -N(OR₂₁)C(Z)NR₈R₉, -N(OR₂₁)C(Z)R₈, -C(=NOR₂₁)R₈, -NR₁₀C(=NR₁₅)SR₁₁, -NR₁₀C(=NR₁₅)NR₈R₉, -NR₁₀C(=CR₁₄R₂₄)SR₁₁, -NR₁₀C(=CR₁₄R₂₄)NR₈R₉, -NR₁₀C(O)C(O)NR₈R₉, -NR₁₀C(O)C(O)OR₁₀, -C(=NR₁₃)NR₈R₉, -C(=NOR₁₃)NR₈R₉, -C(=NR₁₃)ZR₁₁, -OC(Z)NR₈R₉, -NR₁₀S(O)₂CF₃, -NR₁₀C(Z)OR₁₀, 5-(R₁₈)-1,2,4-oxadizaol-3-yl or 4-(R₁₂)-5-(R₁₈R₁₉)-4,5-dihydro-1,2,4-oxadiazol-3-yl;

20 R₅ is hydrogen, C₁-4 alkyl, C₂-4 alkenyl, C₂-4 alkynyl or NR₇R₁₇, excluding the moieties -SR₅ being -SNR₇R₁₇ and -SOR₅ being -SOH;

R₆ is C₁-4 alkyl, halo-substituted-C₁-4 alkyl, C₂-4 alkenyl, C₂-4 alkynyl or C₃-5 cycloalkyl;

25 R₇ and R₁₇ is each independently selected from hydrogen or C₁-4 alkyl or R₇ and R₁₇ together with the nitrogen to which they are attached form a heterocyclic ring of 5 to 7 members which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR₂₂;

R₈ is hydrogen, heterocyclyl, heterocyclylalkyl or R₁₁;

30 R₉ is hydrogen, C₁-10 alkyl, C₂-10 alkenyl, C₂-10 alkynyl, C₃-7 cycloalkyl, C₅-7 cycloalkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl or R₈ and R₉ may together with the nitrogen to which they are attached form a heterocyclic ring of 5 to 7 members which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR₁₂;

35 R₁₀ and R₂₀ is each independently selected from hydrogen or C₁-4 alkyl;

R₁₁ is C₁-10 alkyl, halo-substituted C₁-10 alkyl, C₂-10 alkenyl, C₂-10 alkynyl, C₃-7 cycloalkyl, C₅-7 cycloalkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;

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R₁₂ is hydrogen, -C(Z)R₁₃ or optionally substituted C₁₋₄ alkyl, optionally substituted aryl or optionally substituted aryl-C₁₋₄ alkyl;

R₁₃ is hydrogen, C₁₋₁₀ alkyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;

5 R₁₄ and R₂₄ is each independently selected from hydrogen, alkyl, nitro or cyano;

R₁₅ is hydrogen, cyano, C₁₋₄ alkyl, C₃₋₇ cycloalkyl or aryl;

R₁₆ and R₂₆ is each independently selected from hydrogen or optionally substituted C₁₋₄ alkyl, optionally substituted aryl or optionally substituted aryl-C₁₋₄ alkyl, or together with the nitrogen which they are attached form a heterocyclic ring of 5 to 7 members

10 which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR₁₂;

R₁₈ and R₁₉ is each independently selected from hydrogen, C₁₋₄ alkyl, substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl or together R₁₈ and R₁₉ denote a oxygen or sulfur;

15 R₂₁ is hydrogen, a pharmaceutically acceptable cation, C₁₋₁₀ alkyl, C₃₋₇ cycloalkyl, aryl, aryl C₁₋₄ alkyl, heteroaryl, heteroarylalkyl, heterocyclyl, aroyl, or C₁₋₁₀ alkanoyl;

R₂₂ is R₁₀ or C(Z)-C₁₋₄ alkyl;

R₂₃ is C₁₋₄ alkyl, halo-substituted-C₁₋₄ alkyl, or C₃₋₅ cycloalkyl;

R₃₆ is hydrogen or R₂₃;

20 or a pharmaceutically acceptable salt thereof.

2. The compound according to Claim 1 wherein R₁ or R₂ is an optionally substituted 4-pyridyl or 4-pyrimidinyl.

25 3. The compound according to Claim 2 wherein the optional substituent is C₁₋₄ alkyl or NR₁₀R₂₀.

4. The compound according to any of Claims 1 to 3 wherein R₁ or R₂ is an optionally substituted phenyl.

30 5. The compound according to Claim 4 wherein the one or more optional substituents are independently selected from halogen or methoxy.

6. The compound according to any of Claims 1 to 5 wherein R₃ is X_C or -(CR₁₀R₂₀)_nR₄.

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7. The compound according to Claim 6 wherein R₃ is hydrogen, -(CR₁₀R₂₀)_n(Y₂)_p, -(CR₁₀R₂₀)_n CH₃; and Y₂ is -NR₈R₉ or -NR₁₀C(Z)R₈; and R₄ is an optionally substituted phenyl.

5 8. The compound according to Claim 5 or 6 wherein R₃ is hydrogen, methyl, amino, -NR₁₀C(O)R₈, phenyl, or phenyl substituted by -SR₈ or -S(O)_mR₁₁.

9. The compound according to Claim 1 which is:
5-(3-Methoxyphenyl)-2-methyl-4-(4-pyridyl)oxazole;
10 5-(4-Fluorophenyl)-2-methyl-4-(4-pyridyl)oxazole;
2-Methyl-4-(Phenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-methyl-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-phenyl-5-(4-pyridyl)oxazole;
2-Amino-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole.

15 4-(4-Fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-methylpyrid-4-yl)oxazole;
4-(3,4-Dichlorophenyl)-5-(4-pyridyl)oxazole;
4-(3-Chlorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-(4-methylthiophenyl)-5-(4-pyridyl)oxazole;

20 4-(4-Fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-5-(4-pyridyl)oxazole;
2-Acetamido-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-amino-pyrimidin-4-yl)oxazole; or pharmaceutically acceptable salts thereof.

25 10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound according to any of Claims 1 to 9.

11. A method of treating a cytokine mediated disease in an animal in need thereof which method comprises administering to said animal an effective cytokine mediating amount of a compound according to any of Claims 1 to 9.

30 12. The method according to Claim 11 wherein the cytokine mediated disease is asthma, adult respiratory distress syndrome, stroke, bone reasorption diseases, arthritic joint conditions, and other inflammatory diseases.

35 13. The method according to Claim 11 or 12 wherein the compound is 5-(3-Methoxyphenyl)-2-methyl-4-(4-pyridyl)oxazole;

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5-(4-Fluorophenyl)-2-methyl-4-(4-pyridyl)oxazole;
2-Methyl-4-(Phenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-methyl-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-phenyl-5-(4-pyridyl)oxazole;
5 2-Amino-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-methylpyrid-4-yl)oxazole;
4-(3,4-Dichlorophenyl)-5-(4-pyridyl)oxazole;
4-(3-Chlorophenyl)-5-(4-pyridyl)oxazole;
10 4-(4-Fluorophenyl)-2-(4-methylthiophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-5-(4-pyridyl)oxazole;
2-Acetamido-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-amino-pyrimidin-4-yl)oxazole; or pharmaceutically acceptable salts thereof.

15 14. The method according to any of Claims 11 to 13 wherein the mediation of the disease state is by Interleukin-1 (IL-1).

20 15. The method according to any of Claims 11 to 13 wherein the mediation of the disease state is by Tumor Necrosis Factor (TNF).

16. A method of treating inflammation in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound according to any of Claims 1 to 9.